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DATA EVALUATION REPORT

STUDY TYPE: Acute Inhalation/Rats (81-3)

P. C. CODE: 023102

MRID NUMBER: 414863-01

TEST MATERIAL: Copper Naphthenate Technical

STUDY NUMBER: HUK 769/1

TESTING FACILITY: Hazleton UK
Otley Road
Harrogate, North Yorkshire
England HG3 1PY

SPONSOR: Naphthenates Council
% Mooney Chemicals Inc.
2301 Scranton Road
Cleveland, Ohio 44113

TITLE OF REPORT: Acute Inhalation Toxicity Study - LC₅₀
Rats (4 Hour Exposure)

AUTHOR(S): C.J. Collins

REPORT ISSUED: April 3, 1990

CONCLUSIONS: In this study, no deaths occurred when male and female rats were exposed to an atmosphere of 2.966 mg/l of copper naphthenate (diluted with xylene) for four hours. The mass median aerodynamic diameter of the test atmosphere was 1.71 μ m; the percent of particles less than 1 μ m was 23%. The LC₅₀ for the test material was greater than 2.966 mg/l.

TOXICITY CATEGORY: III

CLASSIFICATION: Guideline - This study satisfies the guideline requirements (81-3) for an acute inhalation study in rats.

I. MATERIALS

A. Test Material

Copper naphthenate (Batch number 24049P) was received at the testing facility on January 29, 1990. The technical material is a deep green viscous oil that is 9.5% copper. It was stored in a sealed container at ambient temperature and humidity in the dark. As supplied, the copper naphthenate was too viscous to be aerosolized so a 60% w/w solution in xylene was used.

B. Test Animals

Sprague-Dawley rats (ten males and ten females) were obtained from Charles River (UK) Ltd., Margate. They were approximately six to eight weeks old and weighed 180 to 200 g. They were housed in suspended stainless steel mesh cages in groups of 5 by sex in rooms where the temperature was 19 to 25°C, the relative humidity was 40 to 70% and there were 12 hours of light/ 12 hours of dark. Food (SQC Rat and Mouse Maintenance Diet No. 1 Expanded) and tap water were provided *ad libitum* except during the exposure period. The testing facility reports that the food and water were analyzed for contaminants and data are on file at the facility. The animals were acclimatized for five days prior to the study initiation.

II. METHODS

Animal Exposure

A group of five male and five female rats had whole body exposures to a nominal concentration of 7.524 mg/l of the test article for four hours. (The actual concentration, as measured during the exposure period, was 2.966 mg/l.) This concentration was the maximum practical in view of the material's potential flammability and toxicity. A control group of five male and five female rats was exposed under similar conditions to an atmospheric concentration of 5 mg/l of xylene. The animals were observed at hourly intervals during the exposure period and then once daily thereafter for clinical signs of toxicity and twice daily for morbidity and mortality during the 14-day observation period. Body weights were recorded immediately before and after exposure, on days 8 and 15 of the study and before necropsy. At necropsy, the lungs, bronchi and trachea were dissected free and weighed together.

Atmosphere Generation

A Sachsse nebulizer located in the top of the recirculation duct of a stainless steel and perspex 1.4 m³ internal whole body exposure chamber was supplied with compressed air and

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used to produce an atmosphere of the test material. The liquid test material was metered to the nebulizer from a reciprocating piston pump. The atmospheres were filtered through an in-line particulate filter, followed by an activated carbon filter before being exhausted and vented to the outside of the building. (See attached Figure 3 for a schematic of the test system.)

Experimental Measurements

The chamber air flow, oxygen concentration, temperature and relative humidity were measured continuously and recorded every half-hour. Hourly samples of the chamber atmosphere were taken by drawing a known volume through an open face glass fibre filter positioned at a site representative of that occupied by the nares of the animals and analyzing it gravimetrically for the concentration of copper naphthenate. The particle size of the test atmosphere was determined hourly using a Sierra Marple Model 298 Cascade Impactor with 6 separation stages corresponding to maximum mass median aerodynamic diameters of 0.52, 0.93, 1.55, 3.50, 6.00 and 9.80 μm . The cumulative percentage by weight of the test substance at each stage was plotted as a probability value against the logarithmic value of the upper class limit of that stage. The point at which the cumulative distribution line crossed the 50th percentile was an estimate of the mass median aerodynamic diameter (MMAD). The nominal concentration of the test material was calculated by multiplying the weight of the formulation used by the % test article in solution and dividing by the product of the flowrate times the duration times 100.

III. RESULTS

Exposure Conditions

The mean gravimetric concentration of the atmosphere was 2.966 mg/l; the nominal concentration was 7.524 mg/l. The measured xylene concentrations for the test and control groups were 5.063 and 5.023 mg/l, respectively. The mass median aerodynamic diameter (MMAD) of the treated atmosphere was 1.71 μm ; the proportion of particles less than 1 μm was 23%. The temperature recorded inside the chamber for the control and treated groups was between 18 and 21° C and the relative humidity was between 38 and 53%. The airflows for both groups were 200 l/min; the oxygen concentration was between 20.6 and 21.1%.

Animal Observations

No animals died during the study. There were treatment-related signs of toxicity on the day of exposure including

piloerection, salivation, nasal secretion, respiratory distress, squinting and staining of the fur. The red stained nasal secretion, piloerection and staining of the fur continued until day 11 of the observation period. No signs of toxicity were observed in the control animals.

The treated animals had a decreased body weight gain but most of the animals had regained their pre-exposure body weight by the end of the study. No treatment-related gross necropsy changes were seen. The mean lung weight and lung/body weight ratios in the treated animals were increased when compared to the control animals.

Signed statements of Quality Assurance and compliance with the Good Laboratory Practice regulations were submitted by the testing facility. The sponsor submitted a Statement of No Data Confidentiality Claims.

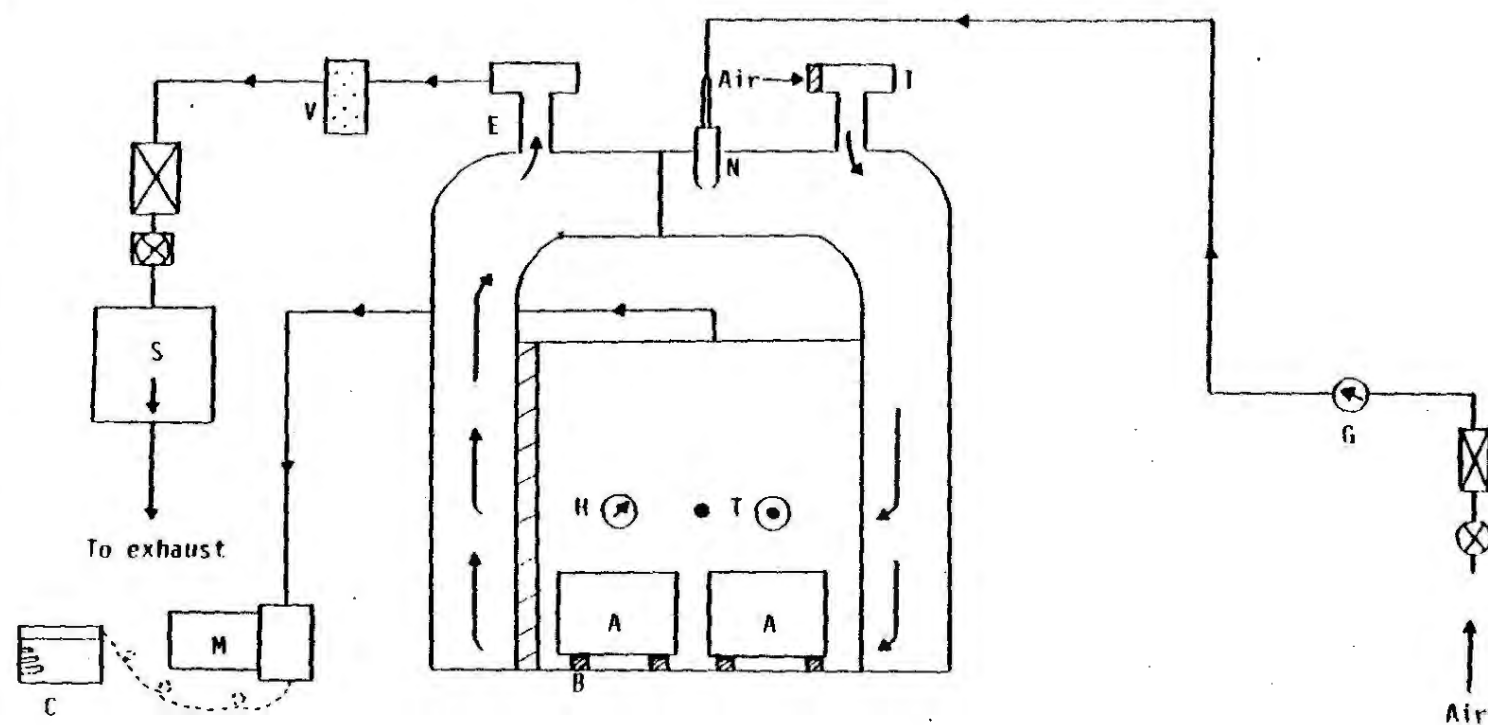
IV. CONCLUSIONS

In this study, no deaths occurred when male and female rats were exposed to an atmosphere of 2.966 mg/l of copper naphthenate (diluted with xylene) for four hours. The mass median aerodynamic diameter of the test atmosphere was 1.71 μm ; the percent of particles less than 1 μm was 23%. The LC_{50} for the test material was greater than 2.966 mg/l.

V. TOXICITY CATEGORY: III

VI. CORE CLASSIFICATION: Guideline

FIGURE 3.
Schematic diagram of exposure system



KEY

- Particulate filter
- A Cages for animals
- Screened cable
- M I.R. gas analyser
- B Cage support

- C Chart recorder
- S Charcoal scrubber
- Direction of air flow
- T Thermometer probe
- H Hygrometer
- Worcester valve
- N Sachsse nebuliser

- Calibrated flowmeter
- Needle valve
- Position of gravimetric sample probe
- I Chamber inlet port
- G Pressure gauge
- V Particulate trap
- E Chamber exhaust port



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Chemical: Copper naphthenate

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